

**REMARKS**

Reconsideration of this Application and entry of the foregoing amendments are requested. The claims have been amended in view of the Office Action of December 9, 1999 to better define what the Applicants consider the present invention, as fully supported by an enabling disclosure.

By the present communication, claims 1 and 12-13 are cancelled, leaving claims 2-11 and 14-22 as pending. New claim 20 replaces claim 1. Support for the amendment is found throughout the application and the claims as initially filed. For example, support for an increase in fluorescence as a result of amplification can be found at page 1, lines 31-34. For claim 18, support for "segment" can be found at page 7, line 29 to page 8, line 2 while support for "hepatitis C virus" can be found at page 7, line 4. Support for new claim 21 can be found at page 3, lines 1-2. Accordingly, the amendments of the claims and new claims raise no issue of new matter.

A new Sequence Listing has been provided because of a discrepancy between SEQ ID NO. 4 in the prior Sequence Listing and Probe C2 in Table III of the specification. The discrepancy has been corrected in the new listing provided herewith. The new Sequence Listing raises no issue of new matter.

The amended paragraph for page 2 starting at line 28 removes the duplicative use of "by."

The amended paragraph for page 3 starting at line 11 replaces the nonsensical term "fwdarw" with the self-evident term "to."

The amended paragraph for page 6 starting at line 25 replaces "gene" with "probe" as supported internally in the amended segment and in the preceding paragraph.

Applicants request that Table I, which was originally filed as page 13 (and also referenced on page 8, line 3 of the specification) be inserted on page 8 between line 3 and Table II. The

Examiner is also directed to the amendment of Table I as indicated in an edited Table I attached to this amendment.

The amended paragraph for page 8 starting below Table IV corrects obvious spelling and punctuation errors.

Accordingly, the amendments to the specification raise no issue of new matter.

### **Rejection Under 35 U.S.C. § 102(e)**

The rejection of claims 1-11 under 35 U.S.C. § 102(e) as allegedly anticipated by Di Cesare (U.S. Patent No. 5,716,784) is respectfully traversed.

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). *See also*, MPEP §2131. The Examiner bears the initial burden of establishing a *prima facie* case of anticipation. Only when a *prima facie* case has been established does the burden shift to the applicant to rebut the *prima facie* case. *See, e.g.*, *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

It is respectfully submitted that Di Cesare does not describe each and every element of the claimed subject matter. For example, the reference fails to disclose a first probe having a quencher molecule capable of quenching the fluorescence of a fluorophore on the second probe. In contrast, Di Cesare, uses an “energy transfer acceptor fluorophore” to receive energy from a donor fluorophore of the other probe.

Thus, when a measurement is required, the PCR reaction mixture temperature is lowered to the Tm of the oligonucleotide detection probe so that annealing of the two probes occurs and energy transfer between the energy transfer donor fluorophore and the energy transfer acceptor fluorophore can result.

U.S. 5,716,784, col. 4, lines 11-17. The acceptor fluorophore in Di Cesare is clearly not a quencher because Di Cesare measures fluorescence emanating from the acceptor fluorophore. See e.g. Col. 6, lines 43-44 ("an measuring the hybridized rhodamine fluorophore emission wavelength oat 600 nm").

Di Casere also fails to disclose monitoring the fluorescence of the fluorophore, wherein an increase in fluorescence correlates with amplification. In contrast to the claimed invention, Di Casere measures a reduction in fluorescence as a result of amplification. This occurs because cleavage of the probes by the 5'-3' exonuclease activity of the polymerase eliminates energy transfer to the acceptor fluorophore that results which results from hybridization of the probes to each other.

Accordingly, as Di Casere does not disclose all of the elements of the claims, reconsideration and withdrawal of the rejection is respectfully requested.

#### **Rejection Under 35 U.S.C. § 112, First Paragraph**

The rejection of claims 1-11 and 13-19 under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter is respectfully traversed. The Examiner alleges that the polymerase in the instant invention "does not necessarily mean that the polymerase is without 5' to 3' exonuclease activity (see p. 3, lines 13-14 of the Office Action) and that "the ratio of the second probe to the first probe is not supported in the specification (see p. 3, lines 14-15 of the Office Action).

As amended, the claims no longer recite the objected limitation. Therefore, Applicants respectfully submit that this rejection has been rendered moot.

#### **The Rejection Under 35 U.S.C. § 112, Second Paragraph**

The rejection of claim 19 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, is respectfully traversed. The Examiner alleges that the abbreviation "HCV" is vague

and indefinite and that the complete name for the term be used (see p. 4, lines 4-5). As amended, the claims now recite the term “hepatitis C virus.” Therefore, the Applicants respectfully request reconsideration and withdrawal of this rejection.

**The 103(a) Rejection Over Di Cesare in view of Hiroaki et al.**

The rejection of claims 1 and 14-18 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Di Cesare in view of Hiroaki et al. (EP 0 461 863 A1), is respectfully traversed. As acknowledged by the Examiner, Di Cesare does not disclose using SEQ ID NO: 1-4 to detect HCV. In an attempt to find a motivation to combine, the Examiner asserts that Hiroaki discloses a nucleotide which comprises SEQ ID NO:1 and 3 and the complementary sequence of SEQ ID NO: 2 and base pair 1-17 of SEQ ID NO: 4 (see p. 5, line 19 to p. 6, line 2 of the Office Action).

Applicants respectfully submit that no *prima facie* rejection has been stated because Hiroaki fails to cure the defects in the teachings of Di Cesare as discussed under the section 102(e) rejection above. As such, the rejection fails to teach or suggest all of the claim limitations. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**The 103(a) Rejection Over Di Cesare in view of Walker et al.**

The rejection of claims 1 and 19 under 35 U.S.C. § 103(a) as allegedly being unpatentably over Di Cesare in view of Walker et al. (U.S. Patent No. 5,270,184) is respectfully traversed. As acknowledged by the Examiner, Di Cesare does not disclose strand displacement amplification method (see p. 7, line 2 of the Office Action). In an attempt to find a motivation to combine, the Examiner asserts that Walker et al. discloses strand displacement amplification method for generating target nucleic acid sequence (see p. 7, line 3 of the Office Action).

Applicants respectfully submit that no *prima facie* rejection has been stated because Walker fails to cure the defects in the teachings of Di Cesare as discussed under the section

102(e) rejection above. As such, the rejection fails to teach or suggest all of the claim limitations. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

### CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to contact the undersigned so that a prompt disposition of this application can be achieved.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date 12/27/2005

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